

National Institute of Allergy and Infectious Diseases / Division of Microbiology and Infectious Diseases	Policy Clinical Quality Management Plan	No.: DMID.OP.QMP001
	Approved: 08-JAN-2008 Effective Date: 14-JAN-2008	Version: 1.0

1.0 **Purpose**

The purpose of this document is to describe the requirements for the development, implementation and evaluation of a Clinical Quality Management Plan (CQMP) at the Division of Microbiology and Infectious Diseases (DMID)- supported clinical research sites conducting clinical research.

2.0 **Scope**

This policy and applicable procedures applies to clinical research sites conducting DMID-supported clinical research.

DMID reserves the right to review site CQMP findings, when applicable.

3.0 **Background**

This policy complies with the National Institute of Allergies and Infectious Diseases (NIAID) Clinical Research Standards. The CQMP describes elements to assist DMID-supported sites in developing, implementing and evaluating such a plan. The requirements listed in this policy are *basic requirements* necessary for clinical research sites to comply with applicable federal and state regulations, International Conference on Harmonization (ICH) E6 Good Clinical Practice (GCP) guidance, and DMID Clinical Terms of Award.

Quality Management (QM) is an overall system of oversight required for the conduct of DMID-supported clinical research. The QM activities facilitate planning for effective protocol implementation, assure compliance with DMID requirements, identify areas in need of corrective action, verify the accuracy of data, and assure a constant state of readiness for an external audit or monitoring visit.

The QM system includes Quality Control (QC) and Quality Assurance (QA). The focus is to provide site staff with the means to identify and resolve problems with protocol implementation and regulatory compliance.

The CQMP should be easy to implement and enables site staff to ensure that the rights and safety of participants are protected, and the data collected are accurate and complete throughout the implementation of the protocol.

4.0 **Definitions**

- Clinical Quality Management Plan (CQMP): A Clinical Quality Management Plan is a formal, written document that encompasses both Quality Assurance and Quality Control procedures and details the responsibility, scope, and frequency of these activities. A CQMP is designed to assess the quality and effectiveness of clinical trials conducted at the site level.
- Corrective Action Plan (CAP): A Corrective Action Plan is a formal, written document that details the implementation of actions taken to detect and eliminate the cause of an area of non-compliance, and prevent reoccurrence of non-compliance.
- Key Quality Indicator (KQI): Key Quality Indicators are selected performance areas and activities that are vital to compliance with accepted standards of performance. For example, all enrollments should be verified for eligibility and proper implementation of the informed consent process.
- Quality Assurance (QA): Quality Assurance is the periodic, systematic, objective and

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comprehensive examination of the total work effort to determine the level of compliance with accepted Good Clinical Practice standards. For example, a monthly review of source documents compared to Case Report Form (CRF) pages to determine adherence to protocol requirements.

- **Quality Audit:** An evaluative process for determining the compliance and/or effectiveness of a process or system. A quality audit is a positive and constructive process intended to identify the activities apt to create problems.
- **Quality Control (QC):** Quality Control is the real time (“day-to-day”) observation and documentation of the sites work processes to ensure that accepted procedures are followed. For example, review of demographic information for accuracy on each Case Report Form (CRF) prior to entry into a database.
- **Quality Management (QM):** Quality Management is the overall system that includes all activities involved in Quality Assurance and Quality Control, including the assignment of roles and responsibilities, the reporting of results, and the resolution of issues identified during the review.
- **Root Cause Analysis:** The process for identifying the most basic or causal factor(s) a problem, inadequate performance, or obstacle to improvement exists.
- **Sample Size:** Sample size is the quantitative selection of items or units (records) from a total population for review.

5.0 **Responsibilities**

Role	Responsibility
Division of Microbiology and Infectious Diseases (DMID)	<ul style="list-style-type: none"> • Notifies Principal Investigator of their responsibility for CQMP development, implementation and evaluation • Reviews findings of CQMP, as applicable.
Clinical Research Site Principal Investigator (PI), or designee Clinical Research staff	<ul style="list-style-type: none"> • Submits CQMP and subsequent revisions to DMID Quality Management team. • Conducts internal Quality Management activities, including corrective actions • Provides CQMP upon request, as applicable.
Office of Clinical Research Affairs (OCRA)	<ul style="list-style-type: none"> • Reviews site/protocol-specific CQMP • Notifies site/Principal Investigator (PI) of CQMP acceptance.
DMID Clinical Trials Management contractor (PPDI)	<ul style="list-style-type: none"> • Assists DMID with review of and recommendations for CQMP plans submitted by DMID-supported clinical research sites/protocols.

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6.0 **Implementation**

DMID clinical research sites are required to develop, implement, and evaluate a CQMP. DMID reviews and accepts the CQMP prior to its implementation.

6.1 **CQMP Submission, Review, and Acceptance - Overview**

6.1.1 **Submission:**

6.1.1.1 The PI or designee is responsible for drafting and submitting a protocol-specific or site CQMP to DMID for review. The CQMP must address the applicable DMID basic requirements.

6.1.1.2 For sites funded through a coordinating center or other network, submission of the site CQMP will be determined with input from the coordinating center or network center, and detailed in coordinating center/network specific processes. These will be negotiated with the coordinating center/network and DMID/OCRA.

6.1.2 **Review:** DMID is responsible for reviewing the CQMP for DMID basic requirements and communicating the review to the PI. This responsibility may be delegated to PPD Quality Services.

6.1.2.1 If CQMP does not meet the basic requirements, findings and recommendations will be communicated to the site via email within fourteen (14) calendar days.

6.1.2.2 DMID clinical research sites / PIs are required to submit CQMP revisions (other than administrative) to DMID.

6.1.3 **Acceptance:** Following resolution of the CQMP review, DMID is responsible for providing a CQMP notification of acceptance to the PI.

6.2 Clinical Quality Management Plan Basic Requirements

6.2.1 **Site and Protocol Identification**

6.2.1.1 Include Protocol Title and Number

6.2.2 **Responsibility**

6.2.2.1 A clearly defined designation of the person(s) responsible for the development, implementation, and evaluation of the CQMP.

6.2.3 **Quality Management Process Description** - The CQMP describes the Quality Assurance and Quality Control activities.

6.2.3.1 Quality Assurance (QA) – The Quality Assurance process determines the type and accuracy of the data reviewed by assessment of the Key Quality Indicators (Section 6.2.4).

6.2.3.2 Quality Control (QC) –The Quality Control activity is a regularly performed and ongoing day-to-day review of 100% of all data collection forms for completeness and logic.

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6.2.3.3 Record Selection - The clinical research site sets a required minimum percentage of records to be reviewed based on, but not limited to, high-risk protocols, high-accruing protocols, initial enrollment in new protocols, and new clinical research staff.

6.2.4 **Key Quality Indicators** - Internal QA review compares source documents, CRFs and protocol to ensure agreement. The following key quality indicators are audited in each subject record selected for review: ([Sample Chart Audit Tool](#))

- 6.2.4.1 Informed consent form and process
- 6.2.4.2 Eligibility criteria
- 6.2.4.3 Test article accountability and administration (if applicable)
- 6.2.4.4 Vaccine preparation procedures (if applicable)
- 6.2.4.5 AE/SAE identification and reporting
- 6.2.4.6 Missed visits, tests, procedures
- 6.2.4.7 Scheduled tests/procedures
- 6.2.4.8 Treatment/study discontinuation
- 6.2.4.9 Reactogenicity (if applicable)
- 6.2.4.10 Other protocol-specific indicators (as determined by the site staff)

6.2.5 **Regulatory File Review** - The review of the Regulatory Files is completed, at a minimum, once during the active study period, or annually if the study is long term, ensuring the contents of the files are complete and up to date.

- 6.2.5.1 Regulatory File Review Tool ([Sample Regulatory File Review Tool](#))

6.2.6 **Test Article Storage, Handling, Accountability and Administration (if applicable)**

The CQMP describes the periodic QM activities that are performed in accordance with the ICH Guidelines for Good Clinical Practice; E6, Section 4.6 Investigational Product(s) addressing test article accountability and administration. Blind for test article must be secured during internal review of these documents and systems. Test Article review activities include, but are not limited to the following *basic requirements*:

- 6.2.6.1 Review and comparison of the Test Article Accountability Logs, Shipping Records, and the Test Article Inventory
- 6.2.6.2 Randomization Code List and Decoding Procedures
- 6.2.6.3 Vaccine Preparation Procedures (if applicable)
- 6.2.6.4 Test Article Storage, Handling, and Labeling Procedures
- 6.2.6.5 Test Article Administration Processes
- 6.2.6.6 Additional Manual of Operations Procedures

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6.2.7 **Tools, Checklists, and Reminders** - The CQMP describes the types of tools, checklists, and reminders used during the QM process. Examples include, but are not limited to, the following:

- 6.2.7.1 Visit Reminder Checklists Chart Audit Worksheets/Tools; ([Sample Chart Audit Tool](#))
- 6.2.7.2 Regulatory File Review Tool (Sample Regulatory File Review Tool)
- 6.2.7.3 Data Entry, Query, or Transmission Reports from the Data Management Center
- 6.2.7.4 Error Reports from Data Management Center (if applicable)
- 6.2.7.5 Clinical Site Monitoring Reports
- 6.2.7.6 Summary Reports from Internal QA/QC Findings ([Sample Quality Management Summary Report Tool](#))
- 6.2.7.7 Other QA/QC Forms

6.2.8 **Staff Training and Competency** - The CQMP describes the processes for ensuring and documenting qualified personnel and competency. Examples include, but are not limited to, the following:

- 6.2.8.1 Institution-Specific Training (i.e., Human Subjects Protection Phlebotomy, Dangerous Goods Regulations, Research staff training, applicable site procedures)
- 6.2.8.2 Protocol-Specific Training (i.e., specimens, test article, data management)
- 6.2.8.3 DMID-Specific Training
 - 6.2.8.3.1 Human Subjects Protection Training (Required)
 - 6.2.8.3.2 Good Clinical Practice Training (Required)
 - 6.2.8.3.3 DMID Regulatory File Document Guidelines
 - 6.2.8.3.4 DMID Source Documentation Guidelines

6.2.9 **Quality Management Summary Reports** - The CQMP describes how findings are summarized, analyzed, and communicated to the staff. The basic elements of the Summary Report include, but are not limited to, the following: ([Sample Quality Management Summary Report Tool](#)).

NOTE: Any safety events or protocol violations which have not been reported previously and independently from a CQMP summary report, should be reported to the site IRB and DMID upon discovery.

- 6.2.9.1 Staff Participation in Audits
- 6.2.9.2 Identification of Problem Areas
- 6.2.9.3 Trend Analysis
- 6.2.9.4 Corrective Action Plan(s)
- 6.2.9.5 Possible Need for Revision to CQMP

6.2.10 **Annual Evaluation of the Clinical Quality Management Plan** – The site staff, including the Principal Investigator, evaluates the CQMP for effectiveness, annually, at a minimum. If the CQMP is modified to increase effectiveness, the submission process is reactivated (Section 6.1).

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7.0 **References**

7.1 **International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use**

7.1.1 **Guidelines for Good Clinical Practice (GCP) E6 (R1)**

7.2 **Office for Human Research Protections**

7.2.1 **Code of Federal Regulations 45 Public Welfare, Department of Health and Human Services Part 46 Protection of Human Subjects**

7.3 **Division of Microbiology and Infectious Disease**

7.3.1 **Regulatory File Guidelines**

7.3.2 **Source Documentation Standards**

8.0 **Inquiries**

Questions or comments regarding this policy may be directed to:

Claudia Baxter, RN, BSN

Nurse Consultant

NIH / NIAID

Division of Microbiology and Infectious Diseases (DMID)

Office of Clinical Research Affairs (OCRA)

Bethesda, MD 20892

baxterc@niad.nih.gov

9.0 **Availability**

This document is available electronically:

NIAID Internet/DMID/Policies and Procedures

<http://www3.niaid.nih.gov/research/resources/DMIDClinRsrch/quality.htm>

DMID Clinical Trials Management contractor (PPD)

<http://www.dmidctm.com/partners/SectionQualityManagement/PageSOPs/SOPs.htm>

An original signed approval is located within the OCRA Clinical Trials Management Section (CTMS) office.

10.0 **Change Summary**

Version Number:	Date of Revision: DD/MM/YY	Replaces:	Effective Date: DD/MM/YY	Description of Revision/Retirement:	Revision Initiated by:
1.0	N/A	N/A	N/A	N/A	N/A